Thus, a further aspect of the present invention relates to a method of treating an individual suffering from a disease associated with hyperproliferating cells which comprises the step of administering to said individual an amount of nucleic acid that comprises a nucleotide sequence that encodes WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof, operably linked to regulatory elements necessary for expression.

Another aspect of the present invention relates to vaccine compositions that comprise a nucleic acid molecule that encodes capsid protein, or immunogenic fragment thereof, from WNV or a other viruses including *Flavivirus* or *Pestivirus*, and a pharmaceutically acceptable carrier or diluent. According to the present invention, genetic material that encodes capsid protein, or an immunogenic fragment thereof, is delivered to an individual in an expressible form. The genetic material, DNA or RNA, is taken up by the cells of the individual and expressed. The capsid protein, or immunogenic fragment thereof, that is thereby produced serves to induce an immune response in the individual. Thus, vaccine compositions comprising genetic material that encodes capsid protein, or an immunogenic fragment thereof, from WNV or other viruses including *Flavivirus* or *Pestivirus*, are useful in the same manner as vaccine compositions comprising capsid protein: for immunizing individuals. The immunity can be prophylactic if the individual is uninfected and therapeutic if the individual is infected. Accordingly, further aspects of the present invention relate to a method of preventing infection or treating infected individuals.

Nucleotide sequences that encode WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof, operably linked to regulatory elements necessary for expression in the individual's cell, may be delivered as pharmaceutical compositions using gene therapy strategies which include, but are not limited to, either viral vectors such as adenovirus or retrovirus vectors or direct nucleic acid transfer. Methods of delivery of nucleic acids encoding proteins of interest, using viral vectors are widely reported. A recombinant viral vector such as a retroviral vector, adenovirus or adeno-associated viral vector is prepared using routine methods and starting materials. The recombinant viral vector comprises a nucleotide sequence that encodes WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof. Such a vector is combined with a pharmaceutically acceptable carrier or diluent. The resulting pharmaceutical preparation may be administered to an individual. Once an individual is infected with the viral vector, WNV or

other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof, is produced in the infected cells.

Nucleotide sequences that encode WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or immunogenic fragments thereof, operably linked to regulatory elements necessary for expression in the individual's cell, may be delivered as vaccine compositions comprising viral vectors, such as adenovirus, adeno-associated virus, vaccinia virus or retrovirus vectors, or bacterial or mycobacterial vectors. Furthermore, the nucleotide sequences can be incorporated within live and/or attenuated vaccines.

Alternatively, a molecule which comprises a nucleotide sequence that encodes WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional or immunogenic fragment thereof, can be administered as a pharmaceutical composition or vaccine by direct nucleic acid transfer, without the use of infectious vectors. The nucleic acid molecule may be DNA or RNA, preferably DNA. The DNA molecule may be linear or circular; it is preferably a plasmid. The nucleic acid molecule is combined with a pharmaceutically acceptable carrier or diluent.

As described above, many aspects of the composition, formulation, dosing, and administration of the pharmaceutical compositions and vaccines of the invention are related, and can be identical. For example, both pharmaceutical compositions and vaccines of the invention may comprise a nucleic acid encoding WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or fragment thereof. The encoded capsid protein, or fragment thereof, in the pharmaceutical composition will be functional in apoptosis activity, whereas, the encoded capsid protein, or fragment thereof, in the vaccine will be immunogenic. Portions of the disclosure concerning related aspects are considered to be relevant to both pharmaceutical compositions and to vaccines.

Importantly, in pharmaceutical compositions, the amount of nucleic acid must be sufficient so that it will be sufficiently expressed to induce cell death. If the nucleic acid encodes a fragment, the fragment must be a functional fragment. The immunogenicity is not a relevant feature in the pharmaceutical composition. In the vaccine compositions, on the other hand, the immunogenicity is critical. The primary activity of vaccines is in the induction of a prophylactic or therapeutic immune response. If a fragment is encoded by the nucleic acid it must be an immunogenic fragment.

According to the invention, the pharmaceutical composition or vaccine comprising a nucleic acid sequence that encodes WNV or a other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof, may be administered directly into the individual. The genetic material is introduced into cells which are present in the body of the individual. Preferred routes of administration include intramuscular, intraperitoneal, intradermal and subcutaneous injection. Alternatively, the pharmaceutical composition may be introduced by various means into cells that are removed from the individual. Such means include, for example, transfection, electroporation and microprojectile bombardment. After the nucleic acid molecule is taken up by the cells, they are reimplanted into the individual. It is contemplated that otherwise non-immunogenic cells that have genetic constructs incorporated therein can be implanted into the individual even if the vaccinated cells were originally taken from another individual.

Genetic constructs may be administered by means including, but not limited to, traditional syringes, needleless injection devices, or "microprojectile bombardment gene guns." According to some embodiments of the present invention, the genetic construct is administered to an individual using a needleless injection device. According to some embodiments of the present invention, the genetic construct is simultaneously administered to an individual intradermally, subcutaneously and intramuscularly using a needleless injection device. Needleless injection devices are well known and widely available. One having ordinary skill in the art can, following the teachings herein, use needleless injection devices to deliver genetic material to cells of an individual. Needleless injection devices are well suited to deliver genetic material to all tissue. They are particularly useful to deliver genetic material to skin and muscle cells. In some embodiments, a needleless injection device may be used to propel a liquid that contains DNA molecules toward the surface of the individual's skin. The liquid is propelled at a sufficient velocity such that upon impact with the skin the liquid penetrates the surface of the skin, permeates the skin and muscle tissue therebeneath. Thus, the genetic material is simultaneously administered intradermally, subcutaneously and intramuscularly. In some embodiments, a needleless injection device may be used to deliver genetic material to tissue of other organs in order to introduce a nucleic acid molecule to cells of that organ.

According to the invention, the genetic vaccine may be administered directly into the individual to be immunized or *ex vivo* into removed cells of the individual which are reimplanted after administration. By either route, the genetic material is introduced into cells which are